



Effect of Prophylactic Transcatheter Arterial Chemoembolization on the Recurrence Rate of Hepatocellular Carcinoma with Microvascular Invasion after R0 Resection

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Abstract

Objective: We investigated the effect of preventive Transcatheter Arterial Chemoembolization (TACE) in preventing recurrence of Hepatocellular Carcinoma (HCC) after R0 resection.

Methods: We retrospectively analyzed recurrence rates over time for 250 cases of HCC after R0 resection, who were divided into patients who underwent TACE (TACE+) and had Microvascular Invasion (MVI+; n=80); TACE+ but did not have MVI (MIV-; n=100); MVI+ but did not undergo TACE (TACE-, n=30); or TACE-/MVI- (n=40).

Results: Among both TACE+ and TACE- patients, MVI- patients had significantly lower recurrence rates at 2(29/100, 29% and 15/40, 37.5%) and 3(40/100, 40.0% and 21/40, 52.5%) years after their procedures than did MVI+ patients (35/80, 43.8% and 20/30, 66.7%; 44/80, 55% and 23/30, 76.7%); the TACE- patients also had lower recurrence rates in the 1st year (9/40, 22.5% vs. 14/30, 46.7%), (all P<0.05). Among MVI+ patients, the TACE+ group had significantly lower recurrence rates at 1(20/80, 25.0%), 2(35/80, 43.8%) and 3(44/80, 55.0%) years than the TACE- group (14/30, 46.7% and 20/30, 66.7% and 23/30, 76.7%), (all P<0.05). Recurrence rates in the MVI-patients tended to be lower at 1(20/100, 20.0%), 2(29/100, 29.0%) and 3(40/100, 40.0%) years for the TACE+ group (9/40, 22.5% and 15/40, 37.5% and 21/40, 52.5%), but not significantly so (all P>0.05).

Conclusion: Recurrence rates for MVI+ patients were significantly higher than for MVI- patients. Postoperative adjuvant TACE may be beneficial for HCC patients with MVI.

Keywords: Hepatocellular carcinoma; Transcatheter arterial chemoembolization; Microvascular invasion; R0 resection; Recurrence

Introduction

Hepatocellular Carcinoma (HCC) is one of the most common malignancies in the world [1,2] and causes about 500,000 deaths every year [3]. Although hepatectomy and liver transplantation are considered to be curative therapies for HCC [1], HCC often relapses after surgery. Transcatheter arterial chemoembolization (TACE) is thought to prevent recurrence, but its efficacy is controversial [4]. Here, we analyzed the effect of TACE on recurrence in 250 patients with HCC who underwent R0 resections.

Materials and Methods

Patients

We followed up 250 patients with HCC who underwent R0 resection between January 2005 and December 2014, over 36 months after their surgeries. Inclusion and exclusion criteria used in this study are shown in Table 1. All patients were informed consent to participate in this study. The trial was registered nationally and approved by our institute ethics committee.

We divided the cohort into four groups: Group 1, who underwent TACE (TACE+) and had Microvascular Invasion (MVI+; n=80); Group 2, who were TACE+ but did not have MVI (MIV-; n=100); Group 3, who were MVI+ but did not undergo TACE (TACE-, n=30); and Group 4, who were TACE-/MVI- (n=40).

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Table 1: Inclusion and exclusion criteria for this study.

Inclusion criteria
16 years ≤ ages ≤ 65 years.
Histopathological classification of high/middle differentiation.
Portal vein tumor free thrombus.
The diameter of a single tumor is more than 3.0 cm and not more than 5.0 cm; All patients are treated with extended resection of the tumor at the margin of cut 2 cm.
Liver function Child-Pugh score not more than 9 points.
Exclusion criteria
Complicated other serious life threatening diseases, such as severe coronary heart disease, other malignant tumor, etc.
Evidence of liver abscess or abdominal infection, biliary fistula, intraperitoneal hemorrhage.
Pregnancy

Table 2: Demographic and clinical data of the four patient groups.

	Group 1	Group 2	Group 3	Group 4	P
N	80 (M/F: 43/37)	100 (M/F: 51/49)	30 (M/F: 17/13)	40 (M/F: 21/19)	
Age (years)	48.62 ± 11.32	46.63 ± 11.61	45.45 ± 11.51	47.55 ± 11.55	>0.05
Complication (%)	0.32 ± 0.13	0.35 ± 0.15	0.33 ± 0.12	0.34 ± 0.14	>0.05
Liver function					
Child-Pugh score	7.5 ± 1.4	7.3 ± 1.5	7.4 ± 1.3	7.4 ± 1.5	>0.05
Tumor diameter (cm)	4.5 ± 1.4	4.3 ± 1.5	4.4 ± 1.3	4.6 ± 1.5	>0.05

MVI: Microvascular Invasion; TACE: Transcatheter Arterial Chemoembolization

Group 1: underwent TACE and had MVI.

Group 2: underwent TACE but did not have MVI.

Group 3: had MVI but did not undergo TACE.

Group 4: did not undergo TACE or have MVI.

TACE

Patients who underwent TACE did so within 1 to 2 months after their hepatectomies (Table 2). The TACE procedure was a “sandwich” method, in which a chemotherapeutic agent (mainly iodide oil) was injected before and after administering chemotherapy. The chemotherapy regimen included fluorouracil, a platin (cisplatin or carboplatin) and Adriamycin (doxorubicin or epirubicin). All patients in this study who underwent prophylactic TACE received only one prophylactic TACE treatment, within 2 months after their surgeries.

Statistical analysis

Statistical analyses were performed using SPSS 16.0 for Windows (SPSS Inc., Chicago, IL). The differences between groups of data were analyzed with the chi-square test (two-tailed). A p-value of <0.05 was considered statistically significant.

Result

The study cohort included 131 males and 119 females. Their average age was 48.01 years (range: 16 to 65 years). Recurrence rates for each patient group, over each time period are shown in Table 3 and 4.

Among both TACE+ and TACE- patients, MVI- patients had significantly lower recurrence rates at 2(29/100, 29% and 15/40, 37.5%) and 3(40/100, 40.0% and 21/40, 52.5%) years after their procedures than did MVI+ patients (35/80, 43.8% and 20/30, 66.7%; 44/80, 55% and 23/30, 76.7%); the TACE- patients also had lower recurrence rates in the 1st year (9/40, 22.5% vs. 14/30, 46.7%), (all P<0.05). Among MVI+ patients, the TACE+ group had significantly lower recurrence rates at 1(20/80, 25.0%), 2(35/80, 43.8%) and 3(44/80, 55.0%) years than the TACE-group (14/30, 46.7% and 20/30,

66.7% and 23/30, 76.7%), (all P<0.05). Recurrence rates in the MVI- patients tended to be lower at 1(20/100, 20.0%), 2(29/100, 29.0%) and 3(40/100, 40.0%) years for the TACE+ group (9/40, 22.5% and 15/40, 37.5% and 21/40, 52.5%), but not significantly so (all P>0.05).

Discussion

Although preventive TACE has become a common post-surgical treatment for HCC [4,5], its efficacy is still controversial. Support for TACE is based on the fact that compressing a tumor during surgery may lead to its spread. Postoperative TACE helps to clear up any proliferating, remnant, or difficult-to-find tumor cells, and thus reduce early recurrence rates [5,6]. A meta-analysis of 4 randomized controlled trials and 3 non-randomized controlled trials concluded that postoperative adjuvant TACE improves survival rates at 2 years and 3 years after resection [7]. The basis for opposing the use of TACE is that TACE can obviously inhibit patients' immune systems, thereby contributing to tumor recurrence and metastasis [8,9]. Our results show that among MVI- patients, TACE+ patients tended to have lower recurrence rates at 1, 2 and 3 years, but not significantly so (P<0.05).

The Milan criteria classify MVI as an independent risk factor for HCC [10] and its presence in the hepatic or portal veins or the bile duct is an accurate predictor of recurrence risk and overall survival in patients with HCC after R0 liver resection and transplantation [11-14]. Postoperative adjuvant TACE may be beneficial for HCC patients with MVI [15].

Our results show that among MVI+ patients, the TACE+ subgroup had lower recurrence rates over 1, 2 and 3 years (P<0.05), which indicates that timely administration of preventive TACE can benefit MVI+ patients.

Table 3: Recurrence rates in patients who underwent (or not) TACE.

	Postoperative time	with MVI	without MVI	P
TACE	12 m	20/80 (25.0%)	20/100 (20.0%)	0.423
	24 m	35/80(43.8%)	29/100 (29.0%)	0.04
	36 m	44/80(55.0%)	40/100 (40.0%)	0.045
Without TACE	12 m	14/30 (46.7%)	9/40 (22.5%)	0.033
	24 m	20/30 (66.7%)	15/40 (37.5%)	0.016
	36 m	23/30 (76.7%)	21/40 (52.5%)	0.038

m: Months; MVI: Microvascular Invasion; TACE: Transcatheter Arterial Chemoembolization

Table 4: Recurrence rates in patients who had (or not) MVI.

	Postoperative time	with TACE	without TACE	P
MVI	12 m	20/80 (25.0%)	14/30 (46.7%)	0.029
	24 m	35/80 (43.8%)	20/30 (66.7%)	0.032
	36 m	44/80 (55.0%)	23/30 (76.7%)	0.038
Without MVI	12 m	20/100 (20.0%)	9/40 (22.5%)	0.742
	24m	29/100 (29.0%)	15/40 (37.5%)	0.328
	36 m	40/100 (40.0%)	21/40 (52.5%)	0.178

m: Months; MVI: Microvascular Invasion; TACE: Transcatheter Arterial Chemoembolization

In conclusion, the recurrence rate of MVI+ patients was significantly higher than that of MVI- patients; however, MVI+ patients may benefit from postoperative adjuvant TACE within 1 to 2 months after R0 resection of HCC.

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